REMARKS

Claims 37-79 are pending in this case. Claims 46, 49, 51-54, 56, 57, 61, and 68-79 have been withdrawn from prosecution and claim 39 has been cancelled. Claim 50 has been amended to clarify the claim language. Support for this amendment can be found, *inter alia*, on page 18, first paragraph; and page 23; fifth and sixth paragraphs. After entering this amendment, claims 37, 38, 40-45, 47, 48, 50, 55, 58, and 62-68 will be pending.

The outstanding issues in the final office action are addressed individually below.

1. The Specification Satisfies The Written Description Requirement

Claims 37-45, 47-48, 50, 55, 58-60, and 62-67 stand rejected as failing to comply with 35 U.S.C. § 112, first paragraph, for failing to describe the subject matter of the claimed invention in such a way as to reasonably convey to one of skill in the art that the inventors were in possession of the claimed invention at the time the application was filed. In particular, the Office Action states that "merely listing pathogens and mentioning virtually every class of molecule that can be found in them does not show that applicant was in possession of all of these molecules" (see Office Action, pg. 4). The Office Action also states that "Applicant has shown no evidence whatsoever that any antigen other than tetanus toxoid is capable of inducing immunity" (see *id.*). Applicants respectfully traverse this rejection.

According to MPEP § 2163, an applicant shows possession of the claimed invention by describing distinguishing identifying characteristics sufficient to show that the applicant was in possession of the claimed invention (*see also Pfaff v. Wells Elecs., Inc.*, 525 U.S. 55, 68 (1998). A specification need not disclose in detail what is conventional or well known to one of ordinary skill in the art (see MPEP § 2163.II.A.3(a)). If skilled artisan would have understood the inventor to be in possession of the claimed invention at the time of filing, even if every nuance of the claims is not explicitly described in the specification, then the written description requirement is met (see *id.*).

Furthermore, adequate written description for a genus requires description of a representative number of species by disclosure of relevant identifying characteristics such as structure or other physical and/or chemical properties (see MPEP § 2163.II.A.3(a)(ii)). The

written description requirement does not require actual reduction to practice or a description of every member of a genus.

Applicants respectfully assert that the specification provides sufficient written description because a representative number of species of the claimed genus have been disclosed in the specification. The specification discloses antigens as being from pathogens, and discloses a list of those pathogens (see Specification, pg. 10). The specification further discloses that the antigens share a particularly defining feature—namely; the antigens are derived from pathogens. Pathogens are defined as entities "which through its presence in or on the body leads to or promotes a pathological states which, in principle, is amenable to or could profit from a preventive, curative, or adjuvant immunotherapy" (see *id.* at Specification, pg. 8, 3rd paragraph). Potential antigens that are obtained from the pathogens are disclosed in the specification, including lipids, carbohydrates, and proteins (see Specification, pg. 25). The species described in the specification, therefore, provide those of ordinary skill in the art with as sufficient range of potential organisms and components obtained from those organisms to allow for one of ordinary skill in the art to recognize that Applicants were in possession of the claimed invention.

Applicants also aver that the specification discloses the generation of antibodies in mice for two of the disclosed species, cholera toxin and tetanus toxoid (see pg. 49, Example 90). This data shows that two different antigens can induce antibody production in mice (see Fig. 14 and pg. 49, Example 90). The induction of an antibody response *in vivo* provides adequate support for the claimed compositions, and allows one of ordinary skill in the art to recognize that Applicants were in possession of the claimed composition.

In addition, Applicants respectfully note that the inclusion of pathogens in which vaccines have not been developed in a list of pathogens that can be used in a vaccine does not show a lack of adequate written description. One of ordinary skill in the art would recognize that all of the pathogens can be utilized to produce a vaccine. Also, the specification discloses data for two such species—cholera toxin and tetanus toxoid (pg. 39, Example 14). That some of the embodiments disclosed have not yielded vaccines is not evidence of a lack of written description. All that is required is that a representative number of species are disclosed to allow one of ordinary skill in the art to recognize that the Applicants were in possession of the claimed invention. This has been accomplished.

The Office Action also appears to be implying that the exact immunoepitope that elicits the response is required. Applicants aver that this is not required for the presently pending claims. The claims are not directed to embodiments requiring identification of a particular epitope. Rather, the claims are generally directed to compositions containing an antigen or mixture of antigens. Applicants therefore aver that, to the extent that the Office Action is requesting identification of particular epitopes, adequate written description does not require such identification.

For all of the reasons stated above, Applicants respectfully request that this written description rejection be reconsidered and withdrawn.

2. The Claims Are Enabled By The Disclosure And The Data Provided Therein

Claims 37-45, 47-48, 50, 55, 58-60, and 62-67 stand rejected under 35 U.S.C. § 112, first paragraph, as not enabling one of skill in the art to make and use the claimed invention. Specifically, the Office Action states that vaccine development is not routine, quoting Ellis, Ch. 29, Vaccines. Plotkin and Mortimer (eds.), 1988 (see pg. 571) ("Ellis") (see Office Action, pp. 7-8). Applicants respectfully traverse this rejection.

According to MPEP § 2164.01, a claimed invention must be enabled so that any person skilled in the art can make and use the invention without undue experimentation. The fact that experimentation may be complex does not make it undue, especially if the art typically engages in such experimentation (MPEP § 2164.01). The test of enablement is not whether any experimentation is necessary, but whether it is undue (MPEP § 2164.01). Moreover, the quantity of experimentation is not undue "since a considerable amount of experimentation is permissible, if it is routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed" (MPEP § 2164.06; *quoting, In re Wands,* 858 F.2d 731, 737 (Fed. Cir. 1988).

As stated in the response dated October 25, 2006, Applicants respectfully assert that the specification amply enables the making and use of the vaccine compositions of the claims because the experiments for determining whether an antigen produces protective immunity require only routine experimentation in light of the disclosure in the specification and the knowledge in the art. For instance, Ellis notes that the technologies for producing proteins allow for rapid production and testing of those proteins (see Ellis, pg. 571). Although Ellis states that

"it is important to realize that recombinant vaccines do not always provide the solution to the problem of prevention," this does not refute the Applicants position, but supports it (see *id.*). The enablement requirement does not require absolute predictability or certainty when teaching how to make and use an invention (MPEP § 2107.03.III, *quoting, In re Wooddy*, 331 F.2d 636, 639 (C.C.P.A. 1964)). Applicants have disclosed the species and potential antigens for use in vaccines, and have shown how antigens from two of those species—cholera toxin and tetanus toxoid—are used to generate an immune response (Ex. 90). Thus, Applicants' specification teaches those of ordinary skill in the art how to make and use the invention.

Moreover, the specification provides data showing that two of the chosen antigens generate an immune response. The specification provides working examples of how to make and use a vaccine from tetanus toxoid and cholera toxin (see Examples 1-28 and 90). It provides detailed examples of how to introduce an antigen into an organism and how to measure the immune response thereto (see Examples 11-15). Furthermore, specific compositions for non-invasive vaccination through the skin are disclosed (see Examples 1-13). The Examples provide sufficient data showing an immune response in two of the organisms disclosed in the specification. Thus, this data shows that the compositions recited in the claims and described in the specification can be utilized to produce vaccines for a wide range of antigens.

Applicants note that the specification teaches those of ordinary skill in the art how to make and use the compositions recited in the claims. The specification also teaches those of ordinary skill in the art how to make and use the compositions containing antigens from two of the species disclosed in the specification. Also, Applicants have taught the range of potential antigens that can be used in the compositions recited in the claims. All that is now left to those of ordinary skill in the art is to obtain the protein from the list provided by the specification, make the composition, and perform challenge experiments using different antigens. This is merely exchanging one reagent for another. Considering that the vaccination field is one of the oldest pharmaceutical fields and the techniques are well-established, the experimentation required to practice the invention is well within the reach of individuals of ordinary skill in art, if not those of *less* than ordinary skill in the art.

Accordingly, Applicants respectfully request that this enablement rejection be reconsidered and withdrawn.

3. The Claims Are Not Indefinite

Claims 37, 39, 44, 47, 50, 58, 60, 65, and 67 stand rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to point out and distinctly claim the subject matter which the applicant regards as the invention. Applicants respectfully traverse these rejections, in part, as explained individually below.

Claim 37 stands rejected as being vague and indefinite because of recitation of the phrase "the penetrant in the form of a minute droplet surrounded by a coating of one or more layers of at least 2 substances that differ by at least a factor of 10 in solubility in a liquid medium" (see Office Action, pp. 9-10). The Office Action further alleges that "[i]f the solubility of these substances differs by a factor of 10,..., the two substances would not form a single layer" (see *id.* at 10).

Applicants respectfully aver that the term is definite. The penetrant is a deformable carrier that has one substance (lipid) that is less soluble than the more soluble substance (surfactant). This is specifically explained in the specification at page 15, 1st paragraph and page 22, last paragraph. The specification also teaches how these substances are mixed to produce the composition recited in the claims (see pg. 35, Example 1).

In light of this explicit disclosure, Applicants are puzzled that the Office Action states that it is incorrect that the two substances can form a single layer. If it is believed that the scientific basis for the claims is incorrect, Applicants request evidence showing that the claim is not feasible. Absent evidence supporting this contention, Applicants aver that this rejection is inappropriate and should be withdrawn on this basis alone.

For all of the reasons stated, Applicants respectfully request that this rejection be reconsidered and withdrawn.

Additionally, Claim 37 stands rejected as being allegedly unclear because "if the antigen or allergen is not actually found in the penetrant, it would not penetrate the skin" (see Office Action, pg. 10). The Office Action also notes that "Applicant asserts that merely mixing the antigen with these penetrant droplets would allow for movement across a bilayer" (see *id.*).

Applicants respectfully assert that Applicants' statements made in their last response have been misconstrued. As an initial matter, Applicants stated that the antigens or allergens

were mixed with the penetrant, *not* that they were mixed with the penetrant *droplets* (see First Response, dated October 25, 2006, pg. 11). Applicants' statement explains that the solution, which is used to form the droplets, was mixed with the antigens or allergens. The claim recites that the penetrant is in the form of a minute fluid droplet surrounded by a coating. The claim further recites that the transdermal vaccine comprises the penetrant, a compound which specifically has or induces cytokine or anti-cytokine activity, and an antigen or mixture of different antigens thereof and/or an allergen or mixture of different allergens thereof. Thus, the claim is clear on its face, and there is a detailed description in the specification about how to make and use compositions covered by the claims, as pointed out in the Office Action (pg. 10).

Accordingly, Applicants aver that as this phrase clearly and distinctly points out the subject matter that is the claimed invention, it is respectfully requested that this rejection be reconsidered and withdrawn.

Claim 39 stands rejected as being vague and indefinite because of the phrase "the antigen or allergen is associated with the penetrant." The Office Action states that it is unclear what other forms of association there can be between the antigen or allergen and the penetrant than those disclosed in Claim 37. The Office Action further states that "Applicant states that "associated is meant to encompass "combined or connected physically with the penetrant" (see Office Action, pg. 11).

In view of the amendment cancelling claim 39, this rejection is moot.

Claim 47 was rejected as being vague and indefinite due to the phrase "derived from." The Office Action acquiesces to the meaning of the term as being "obtained from," then alleges that "the term implies that the antigen has undergone some sort of change" (see *id.*).

As stated in the MPEP, acceptability of claim language depends on whether *one of ordinary skill in the art would understand what is claimed,* in light of the specification (MPEP § 2173.05(b)). In addition, the MPEP further states, "compliance with the requirement for definiteness of 35 U.S.C. § 112, second paragraph, is whether the claim meets the threshold requirements of clarity and precision, *not whether more suitable language or modes of expression are available...[s]ome latitude in the manner of expression and the aptness of terms should be permitted even though the claim language is not as precise as the examiner might desire* (MPEP § 2173.02). Thus, if the claim language is clearly known, as the Office Action has

indicated, and the term is not imprecise, then the claim is allowable under § 112, second paragraph.

Applicants respectfully aver that the phrase "derived from" is not vague and indefinite, because it has an ordinary meaning well known to those of skill in the art, with even the Office Action admitting that the meaning of the term was understood (see Office Action, pg. 12, paragraph 2). The meaning of the term meets the threshold requirements of clarity and precision under § 112, second paragraph. It is therefore irrelevant that there *might* be a definition in which another meaning can be ascribed to the term because those of ordinary skill in the art, as well as laypersons, know the meaning of the term. Applicants have provided a proper definition that is known to those of ordinary skill in art, as well as laypersons, and that is all that is required.

Moreover, the Office Action's allegation that there is an "implied" meaning for "derived from" is of no significance because the Office Action has provided no such definition or evidence that shows that the term can include any such meaning. Hypothetical definitions or implied meanings are not relevant to whether the claims meet the threshold level of precision and clarity to satisfy § 112, second paragraph. Furthermore, even if such another definition is available, there would be no lack of precision because the definition provided for the term is clearly known and understood by those of ordinary skill in the art. Applicants have provided a well-known definition for the term, and therefore, any implications or hypothetical definitions are irrelevant.

The specification also provides support for the meaning of this term. It states that "[i]n one preferred embodiment of the vaccine..., the antigen is derived from a pathogen" such that the "antigen is a part of a pathogen or an allergen in its natural form or after fragmentation or derivatisation" (see Specification, pg. 23, last pargraph, and pg. 10, fourth paragraph). This language indicates that the antigen can be part of the organism, fragmented, or derived from (*i.e.*, obtained from) the pathogen or allergen. This language supports the definition provided by the Applicants, a definition that is sufficiently clear and definite.

Accordingly, Applicants respectfully request that this indefiniteness rejection be reconsidered and withdrawn.

Claim 50 stands rejected as being vague and indefinite due to recitation of the term "compound." The Office Action alleges that the word "each" combined with the word "compound" directs one to more than one compound in claim 37 (see Office Action, pg. 13).

Applicants have amended claim 50 to recited "the compound." Accordingly, Applicants respectfully request that this rejection be reconsidered and withdrawn.

Claims 44, 58, and 60 stand rejected as being vague and indefinite due to recitation of the term "low molecular weight irritant." The Office Action alleges that the term low is not defined in the claim or the specification to provide the requisite degree so that one of skill in the art would be apprised of the scope of the claims. Applicants traverse this rejection.

Applicants respectfully assert that this term is sufficiently described in the specification and would be immediately known to one of ordinary skill in the art. Those of ordinary skill in this art use the term "low molecular weight" frequently to refer to molecules that are of lower molecular weight than other molecules within a particular class (see, *e.g.*, Arts *et al.* (1998) *Toxicol. Appl. Pharmacol.* 152(1): 66-76 (studying the effect of "low molecular weight chemicals" on allergic inflammatory airway reactions and airway morphology and functionality); Frew *et al.* (1996) *Toxicol. Lett.* 86(2-3): 65-72 (reviewing studies on the effects of low molecular weight chemicals on respiratory allergies); Tosti *et al.* (1993)*Toxicol. Ind. Health.* 9(3): 493-502 (studying the effects of allergenic low molecular weight oligomers on skin); Dearman *et al.* (1991) *Int. Arch. Allergy Appl. Immunol.* 95(1): 70-6)). The MPEP states, "acceptability of claim language depends on whether *one of ordinary skill in the art would understand what is claimed,* in light of the specification (MPEP § 2173.05(b)). Consequently, so long as the term is understood by those of ordinary skill in the art, the term is sufficiently definitive.

Applicants also note that the specification provides additional description for the term "low molecular weight irritant." It describes a "low molecular weight irritant" as classes of allergenic metal ions, acids, bases, irritating fluids, (fatty-) alcohols, (fatty-) amines, (fatty-) ethers, (fatty-) sulphonates, -phosphates, etc., or other suitable solvents or amphiphiles (see pp. 25-26). The specification further describes that "only sufficiently small molecules from a large load of...topically deposited haptens can find their way into the skin. Such haptens irritate the organ" and "the problem is most serious with the low molecular weight chemicals or...skin

irritants" (see Specification, pg. 2, last paragraph, *citing*, Cevc *et al.*). The use of the term in the specification appears to comply with the use of the term in the art.

Accordingly, Applicants respectfully request that this indefiniteness rejection be reconsidered and withdrawn.

Claim 65 was rejected as being vague and indefinite because the phrase "pure or purified antigen" utilizes the relative terms "pure or purified." The Office Action alleges that one of skill in the art would not realize to what degree the antigens must be purified (see Office Action, pg. 14). The Office Action further states that the definitions provided by the Applicants "do not agree" (see *id.*).

Applicants respectfully aver that the definitions provided in their response are in fact appropriate and do not conflict. The terms pure and purified are *different,* and should not be ascribed the same meaning or have their meanings compared. The Office Action inappropriately compares the meanings of these *different* terms, even though these terms are clearly directed to describing different types of antigens—those that are pure and those that are purified. The analysis put forth by the Office Action is therefore flawed for this reason alone.

Furthermore, when the definitions for the terms are analyzed, the scope of the claim and the degree of purity required for each term is clear. The term "pure" is known to one of skill in the art as "unadulterated, free from admixture or contamination with extraneous matter" (Stedman's Medical Dictionary, 26th Ed., Williams and Wilkins, 1995). Those of ordinary skill in the art recognize that for something to be pure, it must be unadulterated or free from contamination. This level of purity is well understood in the art as requiring that levels of contamination of extraneous matter be undetectable. The term "to purify" in normal usage is known to one of skill in the art to mean "to remove unwanted constituents from a substance" (McGraw-Hill Dictionary of Scientific and Technical Terms, 5th Ed., McGraw-Hill, New York, 1994). The term "purified" therefore means separated from "unwanted constituents." Thus, "purified" refers to a lower level of purity, requiring only that *unwanted constituents* be removed. A compound can be purified and still have contaminants so long as the *unwanted constituents* (*e.g.*, toxic compounds or compounds that will elicit unwanted immune responses) are removed. Therefore, the degree of purity required from an antigen to be purified or pure is known from the definition, in light of what is known in the vaccine art.

Furthermore, the specification provides methods by which an antigen can be partially purified, and indicates that pure antigen can be obtained from common commercial sources, which provide the degree of antigen purity (Ex. 11-13, pg. 38). Furthermore, Figure 4 shows the effects of antigen purity on antigen efficacy. One of skill in the art would be readily apprised from the teachings of the specification and common knowledge within the art what the term "pure or purified" means and to what degree of purity the claim is referring.

Accordingly, Applicants respectfully request that this indefiniteness rejection be reconsidered and withdrawn.

Claim 67 stands rejected as being vague and indefinite due to the phrase "at least one injectable dose." The Office Action states, "[c]ontrary to applicant's assertion, the specification does not define an "injectable dose"" (see Office Action, pg. 15). The Office Action further alleges that the term "injectable dose" is unclear because "it is not clear what limitations are engendered by the term "injectable dose""(see *id.* at 16). Applicants traverse this rejection.

Applicants respectfully aver that the specification does provide one of ordinary skill in the art with guidance on what is meant by the term "injectable dose." The specification states that "the kit comprises at least *one injectable dose* of the antigen" (see Specification, pg. 27, first paragraph; pg. 28, first paragraph). One of skill in the art would recognize from this description that the term "injectable dose" refers to the dose of the particular antigen injected or that can be injected into a subject. When indicating that a kit comprises at least *one injectable dose*, it is clear that the kit contains a dose—for injection—into a subject.

This meaning is further supported by the definitions for the terms "injectable" and "dose." The term "injectable" means to one of skill in the art "capable of being injected into anything" (Stedman's Medical Dictionary, 26th Ed., Williams and Wilkins, 1995). The term "dose" means to one of skill in the art "the quantity of a drug or other remedy to be taken or applied all at one time or within fractional amounts within a given period of time" (Stedman's Medical Dictionary, 26th Ed., Williams and Wilkins, 1995). It is clear from these definitions that the quantity of an "injectable dose" could be different for every potential individual and treatment regime. However, one of ordinary skill in the art knows that the term means that a particular dose of a vaccine is injected into a subject. There is no need to define the range because those of ordinary skill in the art will determine the dose on a case-by-case basis using

knowledge that has been developed within the art over the last century or longer. Therefore, the term has the requisite level of precision to allow those of ordinary skill in the art to understand that an injectable dose refers to the amount of composition to be taken or applied within a given period by injection into a subject.

Accordingly, Applicants respectfully request that this indefiniteness rejection be reconsidered and withdrawn.

5. Claim Rejections Under 35 U.S.C. § 103

Claims 37, 39-45, 47-48, 50, 55, 58-60, and 62-67 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Glenn *et al.* (PCT Publ., WO 98/20734) ("Glenn") in view of Paul *et al.* (1995) *Vaccine Res.* 4: 145-164 ("Paul"). Applicants traverse this rejection.

For a claimed invention to be obvious under 35 U.S.C. § 103, the references forming the basis for an obviousness rejection must teach or suggest all of the claim limitations of the claimed invention. (*In re Royka*, 490 F.2d 981 (C.C.P.A. 1974)). Even if references and/or the knowledge of those of skill in the art teach or suggest all of the limitations of a claim, an obviousness rejection is overcome by a showing of unexpected results (MPEP § 716.02(a); see also *KSR Int'l. Co. v. Teleflex, Inc.*, 127 S.Ct. 1727, 1740 (2007), *citing*, *Anderson's-Black Rock, Inc. v. Pavement Salvage Co.*, 396 U.S. 57 (1969) (noting that the *Anderson's* Court found a conclusion that a design was not obvious was supported by evidence showing the elements of the design worked together in an *unexpected* and fruitful manner)). In particular, evidence showing a greater than expected result is persuasive of nonobviousness (see *id., citing, In re Corkill*, 711 F.2d 1496, (Fed. Cir. 1985)). An obviousness rejection is also improper where the references teach away from their combination (MPEP § 2145 X.D.2).

Applicants' invention, as recited in Claim 37, is directed to a transdermal vaccine comprising a transdermal carrier, the carrier comprising a penetrant including a minute fluid droplet surrounded by a coating of one or more layers of at least 2 substances. Applicants' claimed transdermal vaccine further comprises a compound that induces cytokine or anti-cytokine activity and an antigen or mixtures of different antigens and/or an allergen or mixtures of different allergens.

Paul teaches transfersome compositions that include bovine serum albumin as the substance that the transfersome is transporting across a barrier. Paul does not teach or suggest a vaccine composition comprising an antigen or allergen that is transported across a barrier. Paul does not teach or suggest the need for additional compounds to co-stimulate an immune reaction (*i.e.*, a compound that induces cytokine or anti-cytokine activity).

Glenn discloses transdermal vaccines of tetanus toxoid and IL-12. Glenn does not teach or suggest improved protective immunity using the transdermal compositions recited in the claims. Moreover, Glenn explicitly distinguishes itself from Paul by explicitly contrasting its invention from the cited art, of which Paul is one of the references cited by Glenn (pg. 3, line 29).

Applicants respectfully aver that the claimed compositions provide surprising, and unexpected, results over what was known in the art—that immunoadjuvants do not necessarily strengthen the immune response when using transdermal immunization (see Paul, pg. 155, third para. and pg. 159, first para.). Paul explicitly sets forth that co-stimulatory factors did not improve the immune response, and teaches that such additional factors were unnecessary to produce an improved, protective immune response (see *id.*). In contrast, Applicants unexpectedly determined that co-stimulatory factors (*i.e.*, compounds that induce cytokine or anti-cytokine activity), in fact, induced an improved protective immune response, which increased the survival rate of tested animals see (see Specification, Fig. 8). These results demonstrate that improved protective immunity can be induced with the addition of co-stimulatory factors to the penetrant composition. Thus, the composition recited in the claims would not have been obvious in view of Paul.

Applicants also respectfully assert that the references teach away from the claimed invention for the reasons stated in the previous response. Briefly, Glenn and Paul both state that it is not possible to immunize epicutaneously with simple protein or peptide solutions and that dermally applied liposomal or mixed micellar immunogens are biologically inactive like simple protein solutions (Paul *et al.*, pg. 145, lines 6-7 and lines 16-18; Glenn *et al.*, page 2, lines 20-28). Both references also teach that dermally applied liposomal or mixed micellar immunogens are "biologically as inactive as simple protein solutions" (see Paul *et al.*, pg. 145, lines 16-18 and

Glenn *et al.* pg. 2, lines 24-28). Accordingly, Glenn and Paul teach away from any combination that would yield the claimed invention.

In addition, Glenn and Paul both teach away from each other because they arrive at *different* and contrasting explanations for transdermal immunization, which would lead one of ordinary skill in the art away from combining the teachings of the references. Paul states, "epicutaneous immunization is governed by the *elastomechanical properties of such agent carriers, primarily by the singularly high deformability and self adaptability of the carrier bodies*" (see Paul, pg. 160, second paragraph). This indicates that transfersomes function as sufficient immunization systems. In contrast, Glenn argues that "*bAREs [bacterial ADP-ribosylating exotoxins] activate Langerhans cells* when applied epicutaneously to the skin in saline solution" and "Langerhans cells direct specific immune responses" (see Glenn, pg. 11, lines 6-9). Glenn, thus, teaches that bAREs are sufficient to immunize a subject. Thus these references describe different and incompatible systems for external application of a compound to generate an immune response. Therefore, not only do the references teach away from any combination that would yield the claimed invention, both references teach competing—and incompatible—mechanisms for epicutaneous immunization.

Applicants further assert that Paul does not demonstrate that the compositions described therein could generate any protective immunity. Paul tests bovine serum albumin, which is not an infectious agent (see Paul, Fig. 3). The authors admit that they have not performed the experiments necessary to show vaccination with full-size proteins across the skin, stating that "we have used bovine serum albumin...to test an astounding new *possibility* for...vaccination...across the skin" (see Paul, pg. 146, third paragraph, emphasis added). Furthermore, the specification of the present application explains that "the generation of a protective immune response was not demonstrated...[in the Paul] publication" (see Specification, pg. 4, first paragraph). Thus Paul discloses compositions containing a non-infectious agent, and does not disclose the necessary experiments to establish that such compositions produced a protective immune response. In contrast, Applicants' application describes experiments performed to show protective immunity for tetanus toxoid, and shows additional experiments causing antibody production for cholera toxin (see Specification, Figs. 4 and 14).

Accordingly, as Paul and Glenn do not render Applicants' claimed invention as obvious, Applicants respectfully request that this § 103 rejection be reconsidered and withdrawn.

Likewise, as dependent Claims 39-45, 47-48, 50, 55, 58-60, and 62-67 contain all of the limitations of independent Claim 37, Applicants respectfully request that their rejection should also be reconsidered and withdrawn.

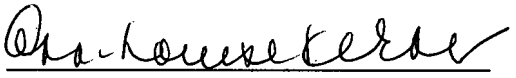
CONCLUSIONS

In view of the arguments set forth above, Applicants respectfully submit that the outstanding rejections contained in the Office Action mailed on July 18, 2007 should be reconsidered and withdrawn.

The time for responding to this action has been extended to November 19, 2007 by the accompanying Petition for a One Month Extension of Time and payment of fee. This application is timely filed because November 18, 2007 fell on a weekend day. No additional fees are believed to be due in connection with this response. However, please charge any underpayments or credit any overpayments to Deposit Account No. 08-0219.

If the Examiner believes that any further discussion of this communication would be helpful, please contact the undersigned at the telephone number provided below.

Respectfully submitted,



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